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• 中文關鍵字	密可納唑；細胞週期停滯；分子機轉；人類癌細胞；抗腫瘤活性；抗黴菌劑
• 英文關鍵字	Miconazole；Cell cycle arrest；Molecular mechanism；Human cancer cell；Antitumor activity；Antifungal agent
• 中文摘要	經過嚴格的篩選過程，我們首度證實部分抗黴菌藥物具有使抑制癌細胞週期停滯的作用，根據其作用位置可分成三大類：(1) 誘發 G0/G1 phase arres ：包括 Ketoconazole ，Fluconazole ，及 Flucytosine 。(2) 誘發 S phase arrest ：Ketoconazole 在低劑量(10 mg/mL)時有大部分細胞停滯於 Sphase 。(3) 誘發 G2/M phase arrest ：如 Griseofulvin ；我們已經證實 Miconazole 造成人類癌細胞週期 G0/G1 週期停滯。已經證實細胞內基因變化爲 p53, p21/Cip1 活化。我們亦證實 Miconazole 有抑制裸鼠腫瘤生長的能力，由於參與細胞週期的基因調控目前已經相當清楚，因此本計劃以有系統的分析方式，逐步探討藥物處理後細胞週期之基因變化情形。
• 英文摘要	In this study, we demonstrated that MIC dose-dependently arrested various human cancer cells at the G0/G1 phase of the cell cycle. The protein levels of p53, p21/Cip1, and p27/Kip1 were significantly elevated by MIC treatment in COLO-205 cells. Electrophoretic mobility gel shift assays (EMSA) showed that the nuclear extracts of the MIC-treated COLO-205 cells exerted a significant binding between wild type p53 and its consensus-binding site present in the p21/Cip1 promoter. These results suggested that the p53-associated signaling pathway is involved in the regulation of MIC-induced cancer cell growth arrest. By immunoblot analysis, we demonstrated that cyclin D3 and cyclin-dependent kinase-4 (CDK4) protein levels were inhibited by MIC-treatment in the cancer cells. Significant therapeutic effect was further demonstrated in vivo by treating nude mice bearing COLO-205 tumor xenografts with MIC (50 mg/kg, i.p.). The protein expression of p53 was significantly increased in MIC-treated tumor tissues by

immunohistochemical staining technique. DNA fragmentation and TUNEL assay were performed and demonstrated that apoptosis occurred in tumor tissues treated with MIC. Our study provides the novel mechanisms of antitumor effects of MIC and such results may have significant applications for cancer chemotherapy.